

Ostenil mini) and triamcinolone (TA; Volon A10) for treatment of osteoarthritis (OA) of the carpometacarpal (CMC) joint of the thumb in a 26-week, controlled, randomized, masked-observer study.

Methods: Patients were treated with three intra-articular injections of either SH (n=28) or TA (n=28). Primary assessments were pain according to VAS and extensive clinical and functional parameters such as swelling, grip power and range of motion. The population was analysed using one- and two-sided Mann-Whitney (MW) estimators.

Results: Maximum pain relief occurred at 2-3 weeks for TA and at week 26 for SH after the first intra-articular injection. At weeks 2-3 TA was significantly better than SH (MW: 0.3319 and 0.3063; p=0.9827 and 0.9929). At week 26 a slight superiority of SH could be observed (MW: 0.53; p=0.3624) and non-inferiority could be proven. After 26 weeks lateral pinch power was significantly better in the SH-group (MW: 0.6331; p=0.0226). In all, 88.0% of patients treated with SH and 79.2% of the TA-group described pain improvement after 26 weeks. No adverse events with causal connection to the investigational products occurred.

Conclusions: We conclude that a single course of three SH injections is effective in relieving pain and improving joint function in patients with OA of the CMC joint of the thumb. Although in comparison with triamcinolone its effects are achieved more slowly, the results indicate a superior long-lasting effect of hyaluronan at 6 months after end of treatment period.

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SUPPRESSION OF TNF- α , IL-1 β , iNOS, AND P38 EXPRESSION BY THE COMBINATION OF AVOCADO SOY UNSAPONIFIABLES, GLUCOSAMINE, AND CHONDROITIN SULFATE IN HUMAN MACROPHAGE-LIKE THP-1 CELLS

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Purpose: The present study determines whether the combination of Avocado Soy Unsaponifiables (ASU), glucosamine (Glu), and chondroitin sulfate (CS) was more effective in suppressing pro-inflammatory gene expression than ASU alone, or Glu and CS together.

Methods: Human monocyte/macrophage surrogate THP-1 cells (5×10^5 cells) were incubated for 24 hrs at 37°C and 5% CO₂ with: (i) control media alone, (ii) ASU (8.3 μ g/ml; NMX1000™-ASU), (iii) Glu (15 mM; FCHG49®) and CS (20 μ g/ml; TRH122®), or with (iv) a combination of ASU (8.3 μ g/ml), Glu (15mM), and CS (20 μ g/ml). All test materials were supplied by Nutramax Laboratories, Inc., Edgewood, MD. The cells were then activated with 20 ng/ml LPS for 1 hour. Total RNA was extracted and subjected to RT-PCR analysis using primers specific to TNF- α , IL-1 β , iNOS, p38, and S14 as the housekeeping gene.

Results: Pre-treatment with the combination of ASU, Glu, and CS profoundly suppressed the expression of TNF- α , IL-1 β , and iNOS by 50-80% in activated THP-1 cells. The combination treatment reduced TNF- α and IL-1 β expression to levels similar to baseline non-activated controls and reduced iNOS expression to levels lower than baseline non-activated levels. The inhibitory effect of the combined preparation on TNF- α , IL-1 β , and iNOS expression is more profound than ASU alone, or Glu and CS together. The inhibition of cytokine and iNOS expression is associated with a profound suppression of p38 expression.

Conclusions: In the present study, we demonstrate that the combination of ASU, Glu, and CS was more effective in suppressing pro-inflammatory gene expression than ASU alone, or Glu and CS together. The combined preparation suppressed TNF- α , IL-1 β , and iNOS expression by downregulating p38, a key signal transduction molecule involved in inflammation. Our present findings suggest the utility of the combination product

to alleviate pain and inflammation in OA patients who may not clinically respond to Glu and CS alone.

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EFFECTS OF HEAT STIMULATION VIA MICROWAVE APPLICATOR ON CARTILAGE METABOLISM AND HSP70 EXPRESSION IN RABBIT KNEE JOINT

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Purpose: Thermotherapy is widely used to conservatively treat joint diseases such as osteoarthritis (OA). While heat stimulation of joints increases pain threshold to alleviate pain, its effects on the articular cartilage have not been clarified. In the present study, heat stimulation was applied to rabbit knee joints to investigate the changes in expressions of heat shock protein 70 (HSP70) and cartilage matrix genes in the articular cartilage in vivo.

Methods: Heat stimulation (0-80 W) was applied to the knee joints of Japanese white rabbits for 20 min using a microwave applicator (2.45-GHz). After 8-72 hrs, the articular cartilage was removed from the knee joints and proteins and total RNA were extracted. As controls, the knee joints without heat stimulation were analyzed. Expression of HSP70 was confirmed by real-time PCR and Western blotting. Expression of proteoglycan core protein and type II collagen were quantified using real-time PCR to assess cartilage matrix metabolism.

Results: Compared to controls, expression of HSP70 mRNA was higher with not less than 40 W of heat stimulation in an intensity-dependent manner. Expressions of proteoglycan core protein and type II collagen mRNA were higher with not less than 20 W of heat stimulation and peaked with 40 W. When quercetin was used to block the increases in HSP70 expression, the expression of proteoglycan core protein mRNA did not increase.

Conclusions: External heat stimulation increased expression of HSP70 in the articular cartilage. This suggested that external heat stimulation reached the articular cartilage. Heat stimulation also increased expression of proteoglycan core protein and type II collagen mRNA in the articular cartilage, indicating increased cartilage metabolism. HSP70 might thus be involved in the increased expression of proteoglycan core protein. With some improvements, heat stimulation might be actively used to protect the cartilage in OA.

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THE EFFICACY AND SAFETY OF CRX-102 - A NOVEL SYNCRETIC DRUG CANDIDATE - IN HAND OSTEOARTHRITIS (HOA): RESULTS FROM A PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL (RCT)

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Purpose: A syncretic drug comprises two compounds that are designed to act synergistically through multiple pathways to provide a novel therapeutic effect, which neither component can achieve alone. The syncretic drug candidate CRX-102 comprises dipyrnidole and low dose prednisolone and is in clinical de-